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**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Paper No. 13

Application Number: 09/083,307
Filing Date: May 22, 1998
Appellant(s): M. Rigdon Lentz

Patrea L. Pabst
For Appellant

# EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed July 12, 2000.

*(1) Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

*(2) Related Appeals and Interferences*

The brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. Therefore, it is presumed that there are none. The Board, however, may exercise its discretion to require an explicit statement as to the existence of any related appeals and interferences.

*(3) Status of Claims*

The statement of the status of the claims contained in the brief is correct.

*(4) Status of Amendments After Final*

No amendment after final has been filed.

*(5) Summary of Invention*

The summary of invention contained in the brief is correct.

*(6) Issues*

The appellant's statement of the issues in the brief is correct.

*(7) Grouping of Claims*

Appellant's brief includes a statement that claims 1-23 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

*(8) Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

*(9) Prior Art of Record*

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

| | | |
|---|---|---|
| 4,708,713 | Lentz | 11/24/1987 |
| 5,523,096 | Okarma et al. | 06/04/1996 |
| 5,861,483 | Wolpe | 01/19/1999 |

Chen et al., "Soluble TNF-alpha receptors are constitutively shed and downregulate adhesion molecule expression in malignant gliomas." Journal of Neuropathology and Experimental Neurology, vol. 56, no. 5 (May, 1997), pp. 541-550.

*(10) Grounds of Rejection*

The following ground(s) of rejection are applicable to the appealed claims:

*Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 8, 9, 16, 18-20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz (4,708,713).

Lentz discloses a method and system for inducing an immune response against diseases and conditions which result from or are dependent upon deficiencies in the immune response system. Such diseases or conditions can be cancer, SIDS, multiple sclerosis, arthritis, as well as other autoimmune diseases. The system includes the filter, inlet and outlet means for connection to a pump, tubing, a pump, and a syringe pump which feeds an anti-coagulant to the system to prevent clotting of the blood (col. 3, lines 56-68). Lentz's method comprises withdrawing blood from a patient, extracorporeally treating the blood to selectively separate components having a low molecular weight, and then returning the blood to the patient to initiate an acute immune response in order to control the disease or condition. The blood is treated by passing through a filter which removes components having molecular weights of less than about 200,000 Daltons (which is well known as an equivalent in the art and is used interchangeably) (col. 2, lines 8-32). Lentz does not disclose removing only components in the blood having a molecular weight of 120,000 Daltons or less. However, Lentz does disclose a device having a filter for removing components having a molecular weight less than 200,000 Daltons which will obviously remove components having a molecular weight of 120,000 Daltons or less. Furthermore, it is taught by Lentz that the filter's pore size may have a range Thus, it would have been obvious to one having ordinary skill in the art to choose a pore size for removing components having a molecular weight of less than 120,000 Daltons since it has been held that where the general conditions of a claim are disclosed in the

prior art, discovering the optimum range involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

With respect to claim 4, the examples of Lentz also discloses multiple treatments for patients in his examples. In example 1 the animal patient underwent three treatments; in example 2 the animal patient was subjected to eight treatments(see table col 7, lines 61-65); and in example 4 a human patient received six treatments (see table in col. 9, lines 1-10).

With respect to claims 8 and 16, the method and system, of claims 1 and 9 respectively, is obvious to one of ordinary skill in the art with respect to Lentz. As with any extracorporeal blood treatment method there is always the possibility for infection. The use of a vaccine or radiation treatment against an infected or diseased tissue is a well know practice in this field. For example, if infection occurs in a patients undergoing extracorporeal treatments an injection or vaccine is given to stop the infection. It was also well known in the art at the time to combine radiation treatment with another method of cancer treatment. Therefore, such combination of Lentz with a vaccine or radiation treatment would have been an obvious choice to make for a person skilled in the art, for example the patient's medical doctor.

With respect to claims 18-20, Lentz teaches that his filter may have an effective pore size of about 0.03-0.07 microns. Further, it is taught that the pores may have sizes or geometries similar to those desired components to be removed from the blood, such as circular or non-circular cross sections (col. 4, line 56-col. 5, line 11).

With respect to claim 22, the system of claim 9 may recirculate plasma as disclosed by Lentz. It is disclosed that plasma can be subjected to the filtration system to remove low molecular weight components (col. 9, line 67-col. 10, line 10).

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz (4,708,713) in view of Okarma et al. (5,523,096). The system of claim 9 having an adsorbent column to remove specific cytokine or cellular inhibitors from the blood is not taught by Lentz. However, Okarma disclosed an extracorporeal system for removing cytokines from the blood with an adsorption matrix (col. 3, line 58-col. 4, line 14). At the time of the invention, it would have been an obvious to combine Lentz with Okarma. The substitution of the adsorbent column for the filter of Lentz, and the removal of cytokines using said column, would have been obvious since both perform an equivalent function, that of removing components from blood. Further, Okarma teaches that the removal of cytokines is done to control the immune system's response to septic shock and other diseases and provide lower circulating levels of cytokine in the blood of a patient.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz (4,708,713) in view of Chen et al. (Journal of Neurology and Experimental Neurology). The method of claim 1 is obvious with respect to Lentz. Lentz does not disclose removing TNF receptor 1 and receptor 2 molecules. However, since TNF receptor 1 and receptor 2

molecules will be soluble in the blood of a patient, they too would be removed. Chen et al. disclosed that TNF receptor 1 and receptor 2 molecules help to evade the immune response against a tumor (pg. 549). Therefore, it would have been obvious toe a person skilled in the art to carry out the method to remove TNF receptor 1 and receptor 2 molecules by filtration since these molecules help to evade the immune response against tumors.

Claims 5, 6, 10-15, 17 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz (4,708,713) in view of Wolpe (5,861,483).

With respect to claims 5, 6, 12, 13, 17 and 23, Lentz discloses a method and system for inducing an immune response against diseases and conditions which result from or are dependent upon deficiencies in the immune response system (see above rejections/arguments for claim 1). Lentz also discloses the use of an anti-coagulant through the device. Lentz does not expressly disclose the device being in a kit and including an agent selected from the group consisting of anti-angiogenic compounds, procoagulant compounds, cytokines, chemotherapeutic agents, and radiation in dosage formulation.

Wolpe, however, discloses the need for stimulatory cytokines, especially erythropoietin, to maintain a fully functional immune system. The methodology that Lentz's method is based on is removing immune inhibitors and letting the body's immune system combat the disease. Therefore, it would have been obvious to a person skilled in the art to add erythropoietin to a kit including Lentz's system since erythropoietin works towards

maintaining a fully functional immune system (col. 1, lines 25-45). The system of Lentz on it's own is comprised of multiple individual pieces (including a filter, inlet and outlet means for connection to a pump, tubing, a pump, and a syringe pump, etc.) and is seen as a kit for performing extracorporeal treatment. As the claims are written such kit limitations are met. With respect to clams 10, 11, 14 and 15, the combination of Lentz and Wolpe disclose the invention except for the use of chemotherapeutic agents, (for example alkylating agents, doxyrubicin, cardoplatinum, cisplatinum, and taxol), procoagulant compounds, or anti-angiogenic compounds. To one of ordinary skill in the art, it would have been obvious to replace the erythropoietin with one of the above listed agents since it has been held to be within the general skill of a worker in the art, such as the physician in charge of the patient's care, to select a known agent or compound on the basis of its suitability for the treatment being performed.

***(11) Response to Argument***

(I)Appellant's argument that the Lentz reference does not teach removal of the "bad" component, which have a "relatively low molecular weight", which is removed by the procedure it is the Examiner's position that the reference does teach such removal. Appellant argues that the invention substitutes a filter with a lower molecular weight cutoff and that Lentz teaches to remove high molecular weight compounds, specifically an IgG immunoglobulin molecule. The Examiner respectfully disagrees.

With respect to the filter not removing components of "relatively low molecular weight," Lentz does in fact teach that the method and system uses a filter having various pore sizes will allow one to separate molecules of various molecular weights. In column 4, line 56- column 5, line 11 examples of different pore sizes and shapes is given for removal of components of various sizes. It is disclosed that a filter having "an effective pore size of about 0.03-0.07 microns will separate components with molecular weights less than about 200,000 Daltons." Further, in column 2, lines 18-33 and in claims 1, 4, 5, 8 and 10, Lentz discloses the removal of "particularly" components having molecular weights less than about 200,000 Daltons.

With respect to Appellant's claim that Lentz teaching toward "a criticality of the higher molecular weight cutoff of the filter, teaching away from" a filter which will remove components having a molecular weight of 120,000 Daltons or less the Examiner also respectfully disagrees. Although Lentz does disclose of filters having the ability to remove components having molecular weights of less than 1,000,000 Daltons, his disclosure also teaches of filters removing smaller components, such as those having a molecular weights less than about 200,000 Daltons. The filter size to remove the larger is disclosed to have pore sizes of about 0.07-0.1 microns and filters to remove the smaller (less than 200,000 Daltons) having pore sizes of about 0.03-0.07 microns. Examples 1 and 3 were carried out using a filter having a pore size of about 0.05 microns, which could not be removing larger components. Furthermore, Lentz teaches of removing components having a molecular weight of less than 200,000 Daltons and the claimed 150,000 Dalton components would obviously be

removed by this system. Thus, as disclosed by the specification and as claimed in claims 1, 4, 5, 8 and 10 it is the position of the Examiner that Lentz does indeed suggests using a filter having a lower molecular weight cutoff and further sets forth a reasonable likelihood that one of ordinary skill in the art would have the ability and knowledge to choose a desired pore size in the range of about 0.03-0.07 microns to filter out a component of a desired molecular weight.

(ii) Appellant's argument that Chen teaches that soluble TNF-alpha receptors, having a molecular weight of 55,000 and 75,000 Daltons in size, is not what Appellant is claiming and that one skilled in the art would be led away from a combination with Lentz and Chen. Further, Appellant argues that there is nothing that would lead one to believe only smaller molecular weight molecules could be removed. The Examiner respectfully disagrees. As stated above, Lentz does teach of a system and method for removing components having a molecular weight of less than 200,000 Daltons. Thus, any components having a molecular weight of less than 200,000 Daltons, including the TNF-alpha receptors, would obviously be removed by the system.

(iii) Appellant argues that Okarma et al. teaches away from the removal of other blood components, stating that only removal of cytokines is sufficient for treating a patient. Appellant also argues that there is nothing that would allow for the combination of Lentz and Okarma. However, the substitution of the adsorbent column for the filter of Lentz, and the removal of cytokines using said column, would have been obvious since both perform an

equivalent function, that of removing components from blood. With respect to Appellant's argument that Lentz does not teach teaches of filters removing smaller components, such as those having a molecular weights less than about 200,000 Daltons, the Examiner disagrees. The filter size to remove the larger is disclosed to have pore sizes of about 0.07-0.1 microns and filters to remove the smaller (less than 200,000 Daltons) having pore sizes of about 0.03-0.07 microns. Examples 1 and 3 were carried out using a filter having a pore size of about 0.05 microns, which could not be removing larger components. Furthermore, Lentz teaches of removing components having a molecular weight of less than 200,000 Daltons and the claimed 150,000 Dalton components would obviously be removed by this system. Thus, as disclosed by the specification and as claimed in claims 1, 4, 5, 8 and 10 it is the position of the Examiner that Lentz does indeed suggests using a filter having a lower molecular weight cutoff and further sets forth a reasonable likelihood that one of ordinary skill in the art would have the ability and knowledge to choose a desired pore size in the range of about 0.03-0.07 microns to filter out a component of a desired molecular weight.

(iv) Appellant argues that Wolpe does not make up for the deficiency of Lentz and that Lentz does not teach of a patient keeping their own immunoglobulin to fight off infection. The Examiner respectfully disagrees. As stated above, Lentz does teach of a system and method for removing components having a molecular weight of less than 200,000 Daltons. Further, it is taught that a range of pore sizes can remove components having molecular weights lower than 200,000 Daltons.

(v) Appellant agues that there is no *prima facie* case of obviousness established or that if there was Appellant would have rebutted such a case by the experimental evidence. For the reasons given above, it is the position of the Examiner that a *prima facie* case has been made and set forth in the previous actions and further explained in this Examiner's Answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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PMB
September 27, 2000

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